第 644 回 難研セミナー

第 220 回 難治疾患共同研究拠点セミナー

下記により難研セミナーを開催しますので、多数御来聴下さい。

記

日　時： 2024 年　6 月 21 日（金）18:00 ～ 19:30

場　所： M&D タワー21 階　大学院講義室 1

演　者： 今道 友純 先生

（Frederick National Laboratory for Cancer Research/ NIH）

演　題： **Recombination of “Defective” Proviruses to Produce Replication-competent HIV-1**

要　旨：

Background: Treatment with complete antiretroviral therapy (cART) leads to "undetectable" levels of plasma virus in the majority of people living with HIV (PLWH). Even the plasma virus cannot be detected; cell-associated "defective" proviral DNA, which contains insertion or deletion (indel) in the genes, complementary RNA transcripts and defective HIV proteins were detected in the cells. The discontinuation of cART led to a delayed reappearance of virus rebound in plasma in a small number of individuals, suggesting that the defect provirus may recombine to form full-length infectious viruses.

Methods: Two distinct defective proviruses, designated SD (lacking nef and gp41) and FD (containing a frame-shifting indel in the RNase H domain of pol) were molecular cloned. The constructs were transfected into 293T or primary CD4(+)-T cells. Supernatants from transfected 293T cells were used to infect MT-2 cells in a syncytia formation assay, while the transfected primary CD4(+)-T cells were co-cultured with PHA-stimulated healthy donor CD4+ T cells for the detection of viral replication by HIV-1 p24 ELISA.

Results: No syncytia formations were observed in MT-2 cell culture when incubated with a combination of 293T-supernatants from SD and FD single transfection (Fig. A). In contrast, abundant syncytia formation was observed in MT-2 cell culture when incubated with a 293T-supernatant from a co-transfection (Fig. B). Similarly, while p24 antigen levels in the mixture of individually transfected CD4(+)-T cells reached only <400 pg/mL, those in the co-cultures of CD4(+)-T cells co-transfected with the two constructs reached >80,000 pg/mL.

Conclusions: The present study provides in vitro evidence of the generation of replication-competent HIV-1 viruses through recombination of defective proviruses. The ability of “defective” proviruses to recombine to form competent viruses may present an additional challenge. In this seminar, a potential mechanism of reappearance of HIV will be discussed.

連絡先：発生再生生物学分野　仁科 博史　（内線 4659）

共催：免疫制御学分野　小松 紀子